REMARKS/ARGUMENTS

1. Remarks on the amendment

Claim 11 has been amended to more specifically define Applicant's claimed invention. Applicant submits no new matter is introduced by the amendment.

2. Response to the Rejection under 35 USC §103(a)

Claims 11-16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Pearlman et al. (WO/9918800) in view of Huet et al. (U.S. 6,426,333). This rejection is respectfully traversed.

Applicant submits that nothing in the art of record teaches or suggests the subject matter defined by the amended independent Claim 11. More specifically, as positively recited in the amended independent Claim 11, the instant dermatological composition consists of an avermectin compound in a concentration from about 0.05% to about 0.1% (w/v) in a lotion consisting of glycerin, hydrogenated polyisobutene, cetearyl alcohol, polyoxyethylene ether of cetyl and stearyl alcohol, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane, stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, citric acid, and water. Therefore, the instant composition does not contain parabens.

It is important to understand the following features and technical advantages of the present invention.

(1) The instant composition contains a very low effective concentration of the active component, namely from about 0.05% to about 0.1% (w/v) of avermectin compound. As demonstrated extensively by examples, at the very low concentration the instant composition is clinically effective, and at the same time it does not cause side effect and can be used for daily treatment for extended period

of time.

(2) The medium of the instant composition is particularly compatible for topical treatment of the dermatological conditions disclosed. As provided previously, Cetaphil® moisturizing lotion is non-comedogenic and does not contain fragrance, lanolins or parabens that could irritate sensitive skin. It is noted that the subject dermatological conditions require repetitive exposure of the affected skin with the composition for extended period of time. Therefore, if any components or combinations thereof in the composition may cause undesired reaction of the skin, the topical treatment would not be successful.

(3) Because of the two effects described above, it has been found that the combination of very low concentration of ivermectin with the specific medium as defined is particularly effective for treating the subject conditions. As described in the Specification, after daily use of the instant composition for up to several months no skin irritation, or increase of skin sensitivity was found (Examples 4-14). It should be particularly pointed out that as shown in many examples the instant composition was applied at bed time to ensure overnight exposure of the affected area to the composition. On the other hand, as further disclosed, the instant composition can be applied to very sensitive areas, such as around the eyes or directly on the eyelids without causing irritation. Therefore, it can be used to treat some clinical conditions, such as perioral dermatitis that affect these sensitive areas.

Applicant points out that Pearlman et al. teach away from the present invention in two aspects.

First, Pearlman et al. teach using Cetaphil® Cleanser itself as the active component because they find Cetaphil® Cleanser is an effective pediculostatic agent. The pertinent section is recited below (p18, line 9-22).

> The most preferred composition for use as a pediculostatic agent in the invention is a mixture of water, cetyl alcohol, propylene glycol, sodium lauryl sulfate, stearyl alcohol, methyl paraben, propylparaben, and butylparaben sold commercially as a nonirritating, non-greasy skin Cleanser under the trademark CETAPHIL® Cleanser (Galderma Laboratories, Inc., Fort Worth, TX).
>
> CETAPHIL® Cleanser is additionally advantageous since it aids in the removal of the nits. While the mechanism for this property is not fully understood, a component or components in CETAPHIL® Cleanser may dissolve or loosen the cement which holds the nits to the hair shaft, and may also make the shaft slippery, thus facilitating the removal of the nits during combing.

As clearly shown in this section, Cetaphil® Cleanser contains three parabens. It is well known that parabens are effective antimicrobials, however, they cause skin irritation. As such, a composition containing paraben is not suitable for treatment of the subject clinical conditions.

Therefore, Pearlman et al.'s specific teaching of using a composition containing three parabens teaches away from the instant composition that requires free of paraben.

The Examiner states that Pearlman et al. teach any commercially available product, such as cleansers, lotions, moisturizers, etc. may be used as the pediculostatic agent. The Examiner further states that Pearlman et al. teach of the use of cleansers and motions/moisturizers interchangeably as pediculostatic agent.

Applicant points out what Pearlman et al. teach is merely a composition that can function as a pediculostatic agent. However, Pearlman et al. does not teach a composition that is suitable for treating subject clinical conditions without causing problems. In fact, the teaching of a composition free of paraben is completely absent in Pearlman et al.

Second, Pearlman et al. specifically teach that the pediculocides active ingredients can be used at levels effective to achieve their intended results of treating head lice infestations, which are at a concentration from about 0.25% to about 2.5% (see page 6, third paragraph). Therefore, contrary to the instant composition, Pearlman et al's method requires a substantially higher ivermectin concentration in order to be effective to treat head lice infestations. It should be noted that the lowest concentration of ivermectin in Pearlman et al.'s composition is more than double of the highest concentration in the instant composition. As such, Pearlman et al. teaches away from the instant composition that has less than half of the lowest concentration in Pearlman et al.

Applicant respectfully points out that the Examiner's reliance on Pearlman et al. in the rejection is contradictory on its own. In paragraphs 5 and 6 of the Office Action, the Examiner states that the reference of Pearlman et al. was not used to teach of the ivermectin concentration of the instant claims but was used to teach of the combination of ivermectin and a pediculostatic agent (i.e., Cetaphil® Cleanser). Instead, Heut et al. was used to teach of formulations comprising ivermectin in concentration of 0.1%. However, in paragraph 14, the Examiner states that the concentrations of Pearlman et al. are from about 0.25% which does not exclude 0.1%.

As stated above, the lowest ivermectin concentration of about 0.25% in Pearlman et al. is more than double of the highest concentration in the instant composition. More specifically, the lowest concentration of 0.25% in Pearlman et al. is 150% higher than the highest concentration 0.1% in the instant composition. Therefore, it is improper to construe that "about 0.1%" would include a concentration 150% higher than it.

The deficiencies of Pearlman et al. are not overcome by Huet et al.

Huet et al teach spot-on formulations for combating parasites, which comprise a combination of a 1-phenylpyrazole derivative (compound A) and a

macrocyclic lactone (compound B) which exhibit synergistic activity against parasites (column 4, lines 17-21). The macrocyclic lactone includes avermectins, ivermectin, abamectin, doramectin, moxidectin, selamectin, milbemycins and their derivatives.

Huet et al specifically teach that a single formulation containing the compounds (A) and (B) in a liquid carrier and in a form which makes possible a single application, or an application repeated a small number of times, will be administered to the animal over a highly localized region of the animal, and it has been discovered that such a formulation is highly effective against ectoparasites and endoparasites (column 9, lines 15-23). Huet et al further teach by example a group of formulations that comprise 10% fipronil (compound A) and ivermectin (compound B) at different concentrations including 0.1%, 0.25%, 0.5% and 1%.

Applicant points out that the effectiveness of Huet et al's formulation in treating parasites depends on the synergistic effects of two active components. In such a composition, the effective concentration of ivermectin (compound B) is provided with the premise of the presence of the primary active component of 1-phenylpyrazole derivative. Therefore, to isolate a specific ivermectin concentration and disregard completely its dependency on the presence of and the effective concentration of the primary active component is inconsistent with the reference's express teaching, and such an isolated ivermectin concentration is meaningless. Hence, the Examiner's reasoning based on Huet et al's concentration is flawed.

It is the present inventor who has discovered that an unusually low concentration of ivermectin from about 0.05% to about 0.1%, in the absence of other active components, is clinically effective in treating the subject conditions, and does not cause irritation, sensitivity, or other side effects. Such a low effective concentration and its significant clinical advantages are not taught by either reference.

Therefore, Applicant respectfully submits that combining these two prior art references to reject Claim 11 of the present application is based simply on the use

of the inventor's disclosure as a blueprint for piecing together prior art to defeat patentability in an improper manner. Only with the hindsight afforded by Applicants' own teaching might one conclude otherwise. Needless to say, such an approach to determining the patentability of an invention is inappropriate and has been frowned upon in numerous decisions by the courts.

In the recent decision in *KSR Int'l Co. vs. Teleflex Inc.*, the Court stated that it is "important to identify a reason that would have prompted a person of ordinary skill in the art in the relevant field to combine the prior art elements" in the manner claimed.

In view of the above, since Pearlman et al teach a composition containing multiple parabens and an effective ivermectin concentration not less than about 0.25%, and Huet et al teach a formula that depends on co-existence of 1-phenylpyrazole derivative and ivermectin, one of ordinary skilled in the art would have no reason to combine these references in order to obtain the instant composition that is free of paraben and has a very low effective concentration in the absence of other active components.

Therefore, Applicant maintains that Applicant's claimed dermatological composition defined in the amended Claim 11 is unobvious in view of the prior art of record.

With regard to Claims 12-16, these claims are dependent upon independent Claim 11. Under the principles of 35 U.S.C. §112, 4th paragraph, all of the limitations of each independent claim are recited in its respective dependent claims. As described above, independent Claim 11 is not obvious, as such Claims 12-16 are submitted as being allowable over the art of record.

Accordingly, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §103(a).

It is respectfully submitted that Claims 11-16, the pending claims, are now in condition for allowance and such action is respectfully requested.

Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

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Date of Signature

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